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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/990,578	11/21/2001	Wallace L. McKeehan	TAMK:2321270.0232.NPUS00	2030

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EXAMINER	
HENRY, MICHAEL C	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 12/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/990,578	MCKEEHAN ET AL.	
	Examiner	Art Unit	
	Michael C. Henry	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-15 are pending in application

Information Disclosure Statement

The information disclosure statement filed complies with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609. It has been placed in the application file and the information referred to therein has been considered as to the merits.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1,2,9,10,12,15 are rejected under 35 U.S.C. 102(b) as being anticipated by Habuchi et al. (US 5,849,722).

In claim 1, applicant claims "A method for isolating anticoagulant heparin or anticoagulant heparan sulfate, the method comprising: contacting an affinity matrix with a mixture comprising anticoagulant heparin or heparan sulfate, wherein the affinity matrix comprises a fibroblast growth factor; and separating the non-bound material from the bound material." Habuchi et al. disclose applicant's method for isolating heparan sulfate, the method comprising: contacting an affinity matrix (bFGF-Sepharose) with a mixture comprising heparan sulfate, wherein the affinity matrix comprises a fibroblast growth factor (bFGF); and separating the non-bound material (which includes some Heparin sulfate) from the bound material (which includes some Heparin sulfate) by washing or elution (col. 8, lines 25-45). It should be noted

that the examiner considers Habuchi et al.s' heparan sulfate to be anticoagulant heparan sulfate, since the anticoagulant property of heparin sulfate is an inherent property.

In claim 2, applicant claims, "The method of claim 1 wherein the fibroblast growth factor preferentially binds to anticoagulant heparin or heparan sulfate compared to non-anticoagulant heparin or heparan sulfate. Habuchi et al. disclose applicant's method of claim 1 wherein the fibroblast growth factor preferentially binds to anticoagulant heparan sulfate compared to non-anticoagulant heparan sulfate (col. 8, lines 25-45). It should be noted that the examiner considers the heparan sulfate that binds to the bFGF-Sepharose be anticoagulant heparan sulfate, since the anticoagulant property of heparin sulfate is an inherent property.

In claim 9, applicant claims "The method of claim 1 wherein the mixture is an anticoagulant drug." Habuchi et al. disclose applicant's method of claim 1 wherein the mixture is an anticoagulant drug (col. 8, lines 25-45). It should be noted that the examiner considers Habuchi et al. heparan sulfate mixture to be an anticoagulant drug, since herparan sulfate is inherently, an anticoagulant.

In claim 10, applicant claims "The method of claim 1 wherein the affinity matrix comprises a fibroblast growth factor immobilized on a support." Habuchi et al. disclose applicant's method of claim 1 wherein the affinity matrix comprises a fibroblast growth factor (bFGF) immobilized on a support (Sepharose) in a column (col. 8, lines 25-45).

In claim 12, applicant claims "The method of claim 1 wherein the non-bound material is separated from the bound material by eluting the non-absorbed material." Habuchi et al. disclose applicant's method of claim 1 wherein the non-bound material (which includes some heparan

sulfate) is separated from the bound material (which include some heparan sulfate) by eluting the non-absorbed material (col. 8, lines 25-45).

In claim 15, applicant claims "A method for separating anticoagulant heparin or anticoagulant heparan sulfate from non-anticoagulant heparin or non-anticoagulant heparan sulfate, the method comprising : contacting an affinity matrix with a mixture comprising anticoagulant heparin or anticoagulant heparan sulfate and non-anticoagulant heparin or non-anticoagulant heparan sulfate, wherein the affinity matrix comprises a fibroblast growth factor that preferentially binds anticoagulant heparin or anticoagulant heparan sulfate compared to non-anticoagulant heparin or non-anticoagulant heparan sulfate; separating the non-bound material from the bound material by eluting the non-bound material from the affinity matrix; desorbing and eluting the bound material from the aftinity matrix. Habuchi et al. disclose applicant's method for separating anticoagulant heparan sulfate from non-anticoagulant heparan sulfate, the method comprising: contacting an affinity matrix (bFGF-Sepharose) with a mixture comprising anticoagulant heparan sulfate and non-anticoagulant non-anticoagulant heparan sulfate, wherein the affinity matrix comprises a fibroblast growth factor (bFGF) that preferentially binds anticoagulant heparan sulfate compared to non-anticoagulant heparan sulfate; separating the non-bound material from the bound material by eluting the non-bound material from the affinity matrix (with water); desorbing and eluting the bound material from the aftinity matrix (with PBS/3M NaCl) (col. 8, lines 25-45). It should be noted that the examiner considers the heparan sulfate that binds to the bFGF-Sepharose be anticoagulant heparan sulfate, and the non-bound heparan sulfate (that is initially washed away or eluted with water) to be, non-anticoagulant.

Claims 1,6,7,8,10, 11,13,14 are rejected under 35 U.S.C. 102(b) as being anticipated by Lormeau et al. (US 5,034,520).

In claim 6, applicant claims 'The method of claim 1 wherein the mixture comprises heparin that is not anticoagulant." Lormeau et al. disclose applicant's method of claim 1 wherein the mixture (di-, tetra-, hexa, octa-, deca-, dodeca- and tetradecasaccharides heparins) comprises heparin (the tetra- or hexa-saccharides) that is not anticoagulant (col. 16, example 8, lines 26-43). It should be noted that lormeau et al. disclose that sub-fraction constituting of fragments of sizes corresponding mainly to 10, 12, 14, 16 and 18 sugar units of heparin possess the pentasaccharide binding site for antithrombine III, and are endowed with a marked anti-factor Xa and a weak, overall anticoagulant activity, and that sub-fraction constituting of fragments of sizes corresponding mainly to 2, 4, 6, 8 and 10 sugar units of heparin, almost completely lack overall anticoagulant activity and exhibiting a very low anti-factor Xa activity. Thus, because the mixture further comprises heparin like tetra- and hexa- which contains 4 and 6 sugar units respectively, then said mixture contains heparin that is not anticoagulant. Claims 7 and 8 which are drawn to the method of claim 1 wherein the mixture comprises crude heparin and low molecular weight heparin, are also encompassed by this rejection, since the said mixture can be considered a crude mixture, and said heparins are of low molecular weight (col. 16, example 8, lines 26-43).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill

in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1,3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lormeau et al. Habuchi et al. (US 5,849,722).

In claim 1, applicant claims "A method for isolating anticoagulant heparin or anticoagulant heparan sulfate, the method comprising: contacting an affinity matrix with a mixture comprising anticoagulant heparin or heparan sulfate, wherein the affinity matrix comprises a fibroblast growth factor; and separating the non-bound material from the bound material." In claim 2, applicant claims "The method of claim 1 wherein the fibroblast growth factor is FGF7."

Habuchi et al. a method for isolating heparan sulfate, the method comprising: contacting an affinity matrix (bFGF-Sepharose) with a mixture comprising heparan sulfate, wherein the affinity matrix comprises a fibroblast growth factor (bFGF); and separating the non-bound material (which includes some Heparin sulfate) from the bound material (which includes some Heparin sulfate) by washing or elution (col. 8, lines 25-45). It should be noted that the examiner considers Habuchi et al.s' heparan sulfate to be anticoagulant heparan sulfate, since the anticoagulant property of heparin sulfate is an inherent property.

The difference between applicants' claimed method and the method of Habuchi et al. is that Habuchi et al. using bFGF whereas the applicant uses FGF7. However, Habuchi et al. disclose, in general, that fibroblast growth factors (FGF) can be used. In fact, heparan sulfate is known to possess binding affinity for several fibroblast growth factors.

It would have been obvious to one having ordinary skill in the art, at the time the claimed invention was made to have used the method of Habuchi et al. to isolate heparan sulfate, and to use any FGF, like FGF7, since Habuchi et al. disclose FGF can be used.

One having ordinary skill in the art would have been motivated, to use the method of the method Habuchi et al. to isolate heparan sulfate, and to use any FGF, like FGF7, since Habuchi et al. disclose FGF can be used.

Claims 1,13,14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lormeau et al. (US 5,034,520).

In claim 1, applicant claims "A method for isolating anticoagulant heparin or anticoagulant heparan sulfate, the method comprising: contacting an affinity matrix with a mixture comprising anticoagulant heparin or heparan sulfate, wherein the affinity matrix comprises a fibroblast growth factor; and separating the non-bound material from the bound material." In claim 13, applicant claims "The method of claim 1 further comprising recovering the anticoagulant heparin." In claim 14, applicant claims "The method of claim 1 further comprising eluting the anticoagulant heparin."

Lomeau et al. disclose A method for isolating heparin, the method comprising: contacting an affinity matrix with a mixture comprising heparin, wherein the affinity matrix comprises a fibroblast growth factor (FGF-separose ® agarose gel); and isolating the chains of the mixture which are endowed with an affinity for FGF (i.e., separating the non-bound material from the bound material (col. 16, example 8, lines 26-43).

The difference between applicants' claimed method and the method of Lormeau et al. is that Lormeau et al. do not disclose recovering or eluting specific anticoagulant heparin chains,

per se. But, Lomeau et al. disclose that heparin in general (i.e. heparin oligosaccharides) can be isolated by separation, and that the sub-fraction constituting of fragments of sizes corresponding mainly to 10, 12, 14, 16 and 18 sugar units of heparin possess the pentasaccharide binding site for antithrombine III, and are endowed with a marked anti-factor Xa and a weak, overall anticoagulant activity. Lomeau et al. also disclose that sub-fraction (separated) constituting of fragments of sizes corresponding mainly to 2, 4, 6, 8 and 10 sugar units of heparin, almost completely lack overall anticoagulant activity and exhibit a very low anti-factor Xa activity (see col. 6, lines 42-56). Furthermore, Lormeau et al. exemplified mixture also contains fractions that contain heparin with 12 and 14 (dodeca- and tetra deca-) sugar units. Thus, Lomeau et al. must have recovered and eluted the heparin containing 12 and 14 (dodeca- and tetra deca-) sugar units which can be considered anticoagulant, since they disclose said heparin binds to

It would have been obvious to one having ordinary skill in the art, at the time the claimed invention was made to have used the method of Lomeau et al. to isolate heparin, comprising recovering and eluting anticoagulant heparin, since Lomeau et al. disclose that said anticoagulant heparin can be isolated by a process comprising recovering and eluting anticoagulant heparin, using the affinity matrix (fibroblast growth factor immobilized on agarose).

One having ordinary skill in the art would have been motivated, to use the method of Lomeau et al. to isolate heparin, comprising recovering and eluting anticoagulant heparin, since Lomeau et al. disclose that said anticoagulant heparin can be isolated by a process comprising recovering and eluting anticoagulant heparin, using the affinity matrix (fibroblast growth factor immobilized on agarose).

Allowable Subject Matter

The following is an examiner's statement of reasons for allowance: The examiner has found claims 3 and 4 to be unobvious over the prior art of record and therefore to be allowable over the prior art of record provided that these claims do not depend on a rejected claim and/or are rewritten in an acceptable form that do not include any new subject matter. The present invention relates a method for isolating anticoagulant heparin or anticoagulant heparan sulfate, the method comprising: contacting an affinity matrix with a mixture comprising anticoagulant heparin or heparan sulfate, wherein the affinity matrix comprises a fibroblast growth factor; and separating the non-bound material from the bound material." The very relevant prior art documents (Habuchi et al., US 5,849,722) and (Lormeau et al.,US 5,034,520) to this invention discloses a similar methods for isolating heparan sulfate and heparin, the methods comprising: contacting an affinity matrix (bFGF-Sepharose) with a mixture comprising heparan sulfate, and contacting an affinity matrix (FGF-Sepharose ® agarose gel) with a mixture comprising heparin, respectively. However, though the methods of the prior art documents are similar to that of the instant invention, the limitations recited in claims 3 and 4 which require the fibroblast growth factor to be a fusion protein and a glutathione-S-transferase-FGF7 fusion protein, is unobvious over the prior art documents.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Henry whose telephone number is 703 308-7307. The examiner can normally be reached on 8:30 am to 5:00 pm; Mon-Fri. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be

reached on 703 308-4624. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308-1235.

MCH

December 8, 2003

SAMUEL BARTS
PRIMARY EXAMINER
GROUP 1600